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I. Status of the Application

Claims 1-8, 10-15 and 37-39 are presently pending in the application. Claims 1-8, 10-15 and 37-39 stand rejected under 35 U.S.C. § 112, first paragraph for various reasons of record. Claims 1-7, 10, 12-15 and 37-39 stand rejected under 35 U.S.C. § 112, second paragraph for various reasons of record. Claims 1-8, 10-15 and 37-39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Lam et al. US Patent No. 5,640,489 (102(e) date of at least 7/2/91) in view of Fodor et al. Science 251: 767 (1991) and applicants' disclosure of the prior art teachings. Claims 1-8, 10-15 and 37-39 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Lam et al. US Patent No. 5,640,489 (102(e) date of at least 7/2/91) in view of Holmes US Patent No. 5,679,773 and applicants' disclosure of the prior art teachings.

Applicants have amended the claims under consideration to more clearly define and distinctly characterize applicants' novel invention. Applicants' respectfully request entry and consideration of the foregoing amendments which are intended to place this case in condition for allowance.

Applicants acknowledge that the application has been filed with informal drawings and will submit formal drawings upon receipt of a notice of allowance.

II. The Rejection of the Claims Under 35 USC § 112, First Paragraph

At page 2 paragraph 3, the Examiner has requested support for the claim language "a label other than a monomer unit of the polymers". In response, applicants' respectfully directed the Examiner to page 3 lines 21-23 where applicants disclose that any detectable label can be used in

addition to isomeric labels; at page 4 line optical isomers are disclosed; at page 4 line 29 a detectable chromogenic moiety, such as a fluorophore, is disclosed; see also the discussion at page 25 line 11 to page 29 line 19 which describe labels of the present invention that are other than monomer units of the polymers, such as external labels. Applicants, therefore respectfully request that the Examiner withdraw his rejection of claim 39.

At page 2 paragraph 4, the Examiner has requested support for the claim language "measuring a property of the mixture". In response, applicants' respectfully submit that measuring the presence of individual components in the mixture via a property of the components (which the Examiner indicates is enabled) is in effect measuring a property of the mixture, as the components make up the mixture. Applicants, therefore respectfully request that the Examiner withdraw his rejection of claims 1-8, 10-15, 37-39.

At page 3 paragraph 5, claims 1-8, 10-15, 37-39 stand rejected as lacking enablement for measuring a property of the mixture of diverse unbound polymers as an indicator of the efficiency of the synthesizing step. In response, applicants respectfully submit that measuring the presence of individual components in the mixture using a property of a label (which the Examiner indicates is enabled) is in effect measuring a property of the mixture, as the components make up the mixture., i.e. one property of the mixture is the distribution of its components. In further support, applicants point out that several methods of analyzing the mixture such as HPLC, standard column chromatography, gel electrophoresis, centrifugation, capillary gel electrophoresis and the like. (See page 3 lines 21-26). In addition, specific HPLC data is provided at Figure 3 for a mixture of

fluorescein labeled polymers including the predominant full length 16-mer. Applicants, therefore respectfully request that the Examiner withdraw his rejection of claims 1-8, 10-15, 37-39.

At page 5 paragraph 8, claims 1-7, 10, 12-15, 37-39 stand rejected as being vague and indefinite with respect to the language "diverse polymers". Applicants respectfully traverse the Examiner's rejection. Applicants' term "diverse" is sufficiently clear in view of applicants' disclosure to include both of the examples presented by the Examiner, namely an array having more than one type of polymer backbone or that the sequence of the monomers is different but only one type of backbone is present. All that is required by applicants' claim is that the polymers be diverse, i.e. namely that there be a variety of polymers. Accordingly, applicants respectfully request that the Examiner withdraw his rejection.

At page 5 paragraph 9, claims 3-5 stand rejected as being vague and indefinite as to the word "size". Applicants respectfully traverse the Examiner's rejection. Applicants' term "size" is sufficiently clear in view of applicants' disclosure and would include the number of monomeric units in the polymer, the mass, a measurement of length or volume depending upon the property being measured by the exemplary analysis techniques disclosed in the specification, namely, HPLC, standard column chromatography, gel electrophoresis, centrifugation, capillary gel electrophoresis and the like. Accordingly, applicants respectfully request the Examiner withdraw his rejection.

At page 6 paragraphs 10 and 11, claims 2 and 15 stand rejected as being vague and indefinite as to the wording "single isomer". Applicants have amended the claims to more clearly set forth and distinctly characterize one embodiment of applicants' invention, namely that including a single optical isomer. Applicants teach at page 19 lines 1-7 that "although essentially any detectable label can be

used, in preferred embodiments the label is monoisomeric, i.e., the label has only a single optical isomer. The use of monoisomeric labels avoids any ambiguity in monitoring the size or charge of polymers in an array caused by having enantiomeric or diastereomeric label. The use of mono-isomeric labels is particularly useful when the detection method is extremely sensitive. For instance, the use of mono-isomeric labels when the detection method is HPLC is particularly preferred.”

Accordingly, applicants respectfully request that the Examiner withdraw his rejection.

At page 6 paragraph 12, the Examiner has rejected claim 39 as being vague and indefinite as to the claim language “a label other than a monomer unit of the polymers”. Applicants respectfully traverse the Examiner’s rejection. Applicants respectfully submit that there is nothing unclear about the phrase “a label other than a monomer unit of the polymers”, i.e. the label is different from the monomeric unit of the polymers is all that is required. Applicants’ respectfully direct the Examiner to page 3 lines 21-23 where applicants disclose that any detectable label can be used in addition to isomeric labels; at page 4 line optical isomers are disclosed; at page 4 line 29 a detectable chromogenic moiety, such as a fluorophore, is disclosed; see also the discussion at page 25 line 11 to page 29 line 19 which describe labels of the present invention that are other than monomer units of the polymers, such as external labels. Applicants also show Figure 2 which show the labeling linker as being different from the polymer. Applicants, therefore respectfully request that the Examiner withdraw his rejection of claim 39.

III. Claims 1-8, 10-15 and 37-39 are Patentable over Lam in view of Fodor

Lam et al US Patent No. 5,650,489 fails to teach or suggest a method of monitoring polymer array synthesis on a solid substrate including (1) the formation of a preselected array of diverse polymers connected to cleavable linkers on a planar surface of solid support, whereby the diverse polymers occupy different regions of the substrate; (2) cleaving diverse polymers from the solid substrate by cleaving the cleavable linkers, thereby creating a mixture of diverse unbound polymers or (3) measuring a property of the mixture of diverse unbound polymers as an indicator of the efficiency of the synthesizing step. Fodor et al. fails to cure the deficiencies of Lam et al. Lam et al provides no motivation that it may be modified in the manner suggested by the Examiner. Example 7 of Lam et al is very clearly directed to the use of resin beads onto which polymers are created (see reference to “solid phase supports”) and not to a planar surface of a solid substrate whereby diverse polymers occupy different regions of the substrate. Lam et al. provide no guidance in Example 7 for creating diverse polymers on a planar surface of a solid substrate or removing the polymers from the planar surface of the solid substrate. Lam et al. therefore provides no reasonable expectation of success of conducting its protocol in Example 7 (even if possible) using a planar surface of a solid support. Accordingly, applicants respectfully request that the Examiner withdraw his rejection.

IV. Claims 1-8, 10-15 and 37-39 are Patentable over Lam in view of Holmes

Lam et al US Patent No. 5,650,489 fails to teach or suggest a method of monitoring polymer array synthesis on a solid substrate including (1) the formation of a preselected array of diverse polymers connected to cleavable linkers on a planar surface of solid support, whereby the diverse

polymers occupy different regions of the substrate; (2) cleaving diverse polymers from the solid substrate by cleaving the cleavable linkers, thereby creating a mixture of diverse unbound polymers or (3) measuring a property of the mixture of diverse unbound polymers as an indicator of the efficiency of the synthesizing step. Holmes et al. fails to cure the deficiencies of Lam et al. Lam et al provides no motivation that it may be modified in the manner suggested by the Examiner. Example 7 of Lam et al is very clearly directed to the use of resin beads onto which polymers are created (see reference to “solid phase supports”) and not to a planar surface of a solid substrate whereby diverse polymers occupy different regions of the substrate. Lam et al. provide no guidance in Example 7 for creating diverse polymers on a planar surface of a solid substrate or removing the polymers from the planar surface of the solid substrate. Lam et al. therefore provides no reasonable expectation of success of conducting its protocol in Example 7 (even if possible) using a planar surface of a solid support. Accordingly, applicants respectfully request that the Examiner withdraw his rejection.

V. C nclusion

Applicants respectfully request entry and consideration of the foregoing amendments and reconsideration and allowance of the case. To the extent the Examiner believes that it would facilitate allowance of the case, the Examiner is requested to telephone the undersigned at the number below.

Respectfully submitted,

Dated: September 20, 1999



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